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09/837,306	04/17/2001	Robert C. Ladner	DYAX/002	9730

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EXAMINER	
EPPERSON, JON D	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 11/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/837,306	LADNER ET AL.	
	Examiner	Art Unit	
	Jon D. Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 September 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *1-6,21,22 and 37-41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7-20,23-36 and 42-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

1. The Response filed September 7, 2005 is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior office action.

Status of the Claims

3. Claims 1-44 were pending. Applicants amended claims 7-10, 12, 14, 16, 20, 26, 28-30, 32, 33, 35 and 42-44. No claims were added or canceled. Therefore claims 1-44 are currently pending.

4. Claims 1-6, 21, 22 and 37-41 are drawn to non-elected species and/or inventions and thus these claims remain withdrawn from further consideration by the examiner, 37 CFR 1.142(b), there being no allowable generic claim.

5. Therefore, claims 7-20, 23-36 and 42-44 are examined on the merits in this action.

6. Please note: This application contains claims 1-6, 21, 22 and 37-41 drawn to a nonelected invention(s). This was addressed in the previous action (see 4/7/05 Non-Final Office Action, paragraph 4). A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Withdrawn Objections/Rejections

7. The objection to claims 12-17 as being in improper multiple dependent form is hereby withdrawn in view of Applicants' arguments and/or amendments. The Enablement Rejection under 35 U.S.C. 112, first paragraph is hereby withdrawn in view of Applicants' arguments and/or amendments. The rejections under 35 U.S.C. 112, second paragraph are withdrawn in view of Applicants' arguments and/or amendments. The Suzuki et al. rejection is withdrawn in view of Applicants' arguments and/or amendments and/or perfection of priority. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

Claims Rejections – 35 U.S.C. 102/103

8. Claims 7-18, 20, 23-36 and 42-44 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Burton et al. (WO 94/07922) (Date of Patent is **April 14, 1994**) (of record).

For ***claims 7-18, 20, 23-36 and 42-44***, Burton et al. disclose a library comprising a collection of genetic packages that display a member of a diverse family of peptides, polypeptides or proteins and collectively display at least a portion of the diversity of the family (e.g., see page 3, Combinatorial Phagemid Libraries Section; see also page 4, lines 6-15, wherein combinatorial libraries of human anti-HIV antibodies are disclosed, "Methods have now been discovered using the phagemid vectors to identify and isolate from combinatorial libraries human monoclonal antibodies that neutralize HIV ..."; see

also figures 5 and 15; see also page 41, section F, especially page 42, lines 18-30, "In one embodiment, the method involves preparing a phagemid library of human monoclonal antibodies by using donor immune cell messenger RNA from HIV infected donors ... Alternatively, the library can be synthetic, or can be derived from a donor who has an immune response to other antigens"). Although Burton et al. do not disclose that their libraries are formed by the same method steps as recited in claims 7-18, 20, 23-36 and 42-44, the products of Burton et al. appear to be the same as those recited by the instant claim, regardless of their method of manufacture (e.g., see MPEP 2113) i.e., a genetic package with a diverse family of peptides, polypeptides or proteins is displayed in each case.

For ***claims 10-17***, Burton et al. disclose the display of human antibodies with light/heavy chains including Fab and FR1 regions (e.g., see page 43, lines 19-23, "For example, the heavy (H) chain and light (L) chain immunoglobulin molecule encoding genes can be randomly mixed (shuffled) to create new HL pairs in an assembled immunoglobulin molecule"; see also page 44, lines 9-13, "In addition, the monoclonal antibodies are human because the H and L chain encoding genes are derived from human immunoglobulin producing immune cells, such as spleen, thymus, bone marrow, and the like"; see also figures 6-13 wherein recombinant Fabs are disclosed; see also figure 10 wherein FR1 is disclosed).

For ***claims 18***, Burton et al. disclose acquired autoimmuno-deficiency syndrome (e.g., see page 18, lines 3-4).

For ***claim 20***, Burton et al. disclose spleen, bone marrow, etc. (e.g., see page 42, lines 18-30, especially lines 28-30, "Alternatively, the library can be ... derived from a donor who has an immune response to other antigens"; see also page 44, lines 9-13, "In addition, the monoclonal antibodies are human because the H and L chain encoding genes are derived from human immunoglobulin producing immune cells, such as spleen, thymus, bone marrow").

The libraries of Burton et al. meet all of the limitations of the claimed library (see above) except for the product-by-process limitations and thus would either anticipate or render obvious the claimed library. See MPEP § 2113, "'[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product do not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process.' *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985)." Here, Applicants claims are drawn to a combinatorial library (i.e., a product), but are defined by various method steps that produce said library and, as a result, represent product-by-process claims. Thus, the process limitations do not appear to provide any patentable weight to the claimed invention in accordance with MPEP § 2113. One of ordinary skill would expect the library of genetic packages to be the same no matter how it was synthesized.

Response

9. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered (and are incorporated in their entirety herein by reference) but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue, "Burton uses amplification primers that are complementary to the 'native' DNA being used to make the library ... Burton, therefore, prevents maximum diversity from being achieved because the 'native' DNA that binds to the primer cannot be substantially diverse ... [furthermore, this claimed method] also remove[s] all unwanted 5' nucleotides leading to consistent expression and display" (e.g., see 9/7/04 Response, page 33, paragraph 1).

This is not found persuasive for the following reasons:

First, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., maximum diversity, consistent expression and display, etc.) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Here, Applicants claims only require that the displayed peptides, polypeptides or proteins be "encoded at least in part" by the claimed method. Thus, the "full diversity" and or "consistency" need not be retained. In addition, the claims do not state how said sequences will be expressed (i.e., there is no expression step) and whether or not they will be further modified to

produce the collection of phage that display a member of a diverse family of peptides, polypeptides or proteins.

Second, the "maximum diversity" to which Applicants' refer must ultimately depend on the sequences that are being amplified (e.g., the DNA). However, Applicants do not place any limit on the structure and/or sequence of the DNA. Thus, a library of any size and/or composition could be created depending on the size and/or nature of the DNA used to create the library. Therefore, Applicants' arguments are not commensurate in scope with the claims.

Accordingly, the 35 U.S.C. § 102(b) rejection cited above is hereby maintained.

Double Patenting

10. Claims 7-20, 23-36 and 42-44 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-116 of copending Application No. 10/045,674 (Pub. No.: US 2003/0232333 A1) (referred to herein as '674). Although the conflicting claims are not identical, they are not patentably distinct from each other because the examined claims are either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1986). For example, claims 7-20, 23-36 and 42-44 of the present application represent overlapping embodiments to all that is recited in claims 1-116 of '674. That is claims 1-116 of '674 either anticipate or render obvious the claims of the present application.

Specifically, both applications claim **[1]** a library comprising a collection of genetic packages (e.g., compare claim 7 of the present application to claims 11-13, 17, 18, 59, 62, 103,

114 of '674, especially claim 12), **[2]** genetic packages that display a member of a diverse family of peptides polypeptides or proteins wherein at least a portion of the diversity of said family is displayed (e.g., compare claim 7 of the present application to claims 11, 12, 13, 59, 62, 103, 114 of '674, especially claim 12), **[3]** displayed peptides, polypeptides, or proteins being encoded at least in part by a nucleic acid that has been cleaved at a desired location (e.g., compare claim 7 of the present application to claims 3, 4, 12, 13 and 99 of '674, especially claim 12), **[4]** contacting the nucleic acid with a single-stranded oligonucleotide, the oligonucleotide being functionally complementary to the nucleic acid in the region in which cleavage is desired (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 and 108 of '674, especially claim 12), **[5]** including a sequence that with its complement in the nucleic acid forms a restriction endonuclease recognition site that on restriction results in cleavage of the nucleic acid at the desired location (e.g., compare claim 7 of the present application to claims 1, 3, 5, 7, 9, 12, 15, 59, 60, 103 and 104 of '674, especially claim 12), **[6]** cleaving the nucleic acid solely at the recognition site formed by the complementation of the nucleic acid (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 59, 60, 103 and 104 of '674, especially claim 12), **[7]** the contacting and the cleaving steps being performed at a temperature sufficient to maintain the nucleic acid in substantially single-stranded form (e.g., compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12), **[8]** the oligonucleotide being functionally complementary to the nucleic acid over a large enough region to allow the two strands to associate such that cleavage may occur at the chosen temperature and at the desired location (e.g., compare claim 7 of the present application to claims 1-13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12). Finally, both

applications also disclose the cleavage site being carried out using a restriction endonuclease that is active at the chosen temperature (e.g., compare claim 7 of the present application to claims compare claim 7 of the present application to claims 1-10, 12, 13, 15, 16, 54, 59, 60, 99-104 of '674, especially claim 12). Thus, claim 7 of the present application is anticipated by claim 12 of '674 and overlaps in scope with the other claims as outlined above.

In addition, both applications disclose **[9]** the use of "DNA sequences" to encode the diverse family of displayed peptides, polypeptides or proteins (e.g., compare claim 8 of the present application to claims 12, 13, 15 and 16 of '674), **[10]** contacting the nucleic acid with a partially double-stranded oligonucleotide (e.g., compare claim 9 of the present application to claims 2, 4, 6, 8, 10, 13, 16, 54, 59, 60, 99-104, 108 of '674), **[11]** the use of Type II-S cleavage sites (e.g., compare claim 9 to claims 19, 52 and 53 of '674), **[12]** the use of immunoglobulins (e.g., compare claim 10 of the present application to claims 21, 22, 23, 26, 28, 36, 65, 75, 92 and 94 of '674), **[13]** Fab or single chain Fv (e.g., compare claim 11 of the present application to claims 22 and 70 of '674), the use of the heavy chain (e.g., compare claim 12 of the present application to claims 23, 24, 25, 68, 71, 80, 81 of '674), **[14]** human FR1 (e.g., compare claims 14 and 15 of the present application to claim 27 of '674), **[15]** the use of a light chain (e.g., compare claim 16 of the present application to claims 28, 29, 67, 70, 82 and 83 of the present application), **[16]** wherein the nucleic acid sequences are at least in part derived from patients suffering from at least one autoimmune disease (e.g., compare claim 19 of the present application to claims 30, 31 and 85 of '674), **[17]** including diseases like lupus (e.g., compare claim 19 of the present application to claim 31 of '674), **[18]** nucleic acid that is isolated, for example, by peripheral blood cells (e.g., compare claim 20 of the present application to claim 32

of '674), **[19]** a temperature between 55 and 60°C (e.g., compare claims 23-25 of the present application to claims 39-42 of '674), the length of the single-stranded oligonucleotide between 17 and 30 bases (e.g., compare claims 26-27 of the current application to claims 43, 44, 49, 55, 56, 109 and 110 of '674), **[20]** the use of endonucleases like BsaJI 9 (e.g., compare claim 28 of the present application to claim 45 of '674), **[21]** the use of partially double-stranded oligonucleotide between 18 and 20 bases (e.g., compare claims 30-32 of the present application to claims 47, 48, 50, 51, 55-58 and 109-112 of '674) and **[22]** partially double stranded region formed by stem and its palindrome (e.g., compare claim 33 of the present application to claims 50 and 52 of '674).

Furthermore, it would have been obvious to one having ordinary skill in the art to modify embodiments of '674 that fall outside the scope of the present application to select a specifically disclosed embodiment that falls within the scope of the present application because these embodiments describe similar and/or identical libraries. One having ordinary skill in the art would have been motivated to do this because these embodiments are disclosed as being preferred embodiments and the dependent claims of '674 teach toward Applicants' claimed invention.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response

11. Applicant's arguments directed to the above double patenting rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above

rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that they are willing to file one or more terminal disclaimers upon allowance of any of the conflicting claims in this application (e.g., see 9/7/05 Response, page 34, paragraph 1).

This is not found persuasive for the following reasons:

The provisional rejection will not be held in abeyance (e.g., see MPEP § 804 B. Between Copending Applications—Provisional Rejections, "The 'provisional' double patenting rejection ***should continue to be made by the examiner*** in each application as long as there are conflicting claims in more than one application unless that "provisional" double patenting rejection is the only rejection remaining in one of the applications."). Here, a double patenting rejection is NOT the only rejection remaining in one of the applications and thus the double patenting rejection is proper.

Accordingly, the double patenting rejection cited above is hereby maintained.

New Rejections

Claims Rejections – 35 U.S.C. 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

14. Claims 7-20, 23-36 and 42-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Burton et al. (WO 94/07922) (Date of Patent is **April 14, 1994**) (of record) and Hoet et al. (Hoet, et al. "The Importance of the Light Chain for the Epitope Specificity of Human Anti-U1 Small Nuclear RNA Autoantibodies Present in Systemic Lupus Erythematosus Patients" *Journal of Immunology* **1999**, *163(6)*, 3304-3312).

For ***claims 7-18, 20, 23-36 and 42-44***, Burton et al. teach all the limitations stated in the 35 U.S.C. 102(b)/103(a) rejection above (incorporated in its entirety herein by reference), which anticipates and, as a result, renders obvious claims 7-18, 20, 23-36 and 42-44.

The prior art teaching of Burton et al. differ from the claimed invention as follows:

For ***claim 19***, Burton et al. fail to disclose nucleic acid sequences that are derived from patients suffering from lupus (e.g., see claim 19).

However, Hoet et al. teach the following limitations that are deficient in Burton et al.:

For ***claim 19***, Hoet et al. (see entire document) teach the use of Lupus patients (e.g., see abstract, "We describe the isolation of the first human anti-U1 RNA autoantibodies [derived] from a combinatorial IgG library made from the one marrow of a systemic lupus erythematosus patient").

It would have been *prima facie* obvious to one skilled in the art at the time the invention was made to derive nucleic acid sequences from patients with rheumatoid arthritis as taught by Hoet et al. to express phage display libraries as taught by Burton et al. because Hoet et al. explicitly state that this can be done (e.g., see Hoet et al., abstract, "We describe the isolation of the first human anti-U1 RNA autoantibodies [derived] from a combinatorial IgG library made from the one marrow of a systemic lupus erythematosus patient"). Furthermore, one of ordinary skill in the art would have been motivated to use lupus patients because Hoet explicitly states that "Ab titers correlate with disease activity" and that the phage library can be used to "underscore the important role of the light chain in the RNA-recognizing specificity of the Abs" (e.g., see abstract; see also page 3305, column 1, paragraph 1). Finally, one of ordinary skill in the art would have reasonably expected to be successful because Hoet et al. disclose a successful example of using a lupus patient (e.g., see Hoet et al., Materials and Methods, Library construction section; see also Results).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D Epperson whose telephone number is (571) 272-0808. The examiner can normally be reached Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jon D. Epperson, Ph.D.
November 26, 2005

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